

MAKING A MOVE ON PHARMA

A pharmaceutical company can have a number of positive effects for the area in which it is located and the incentives to move to certain areas can be very attractive. Barry Mansfield investigates the mitigating factors that need to be considered before the decision to locate is made.

KEY POINTS

- Each new pharma job adds 5.7 jobs to the overall economy.
- Tax laws and local talent are top priorities.



When a strategic business decision is made for the relocation or expansion of a manufacturing facility, the decision itself is often the easiest part of the entire project. There are many considerations that have to be addressed before embarking on such a project; site selection, regulation, environmental impact and providing equipment and furniture are each major tasks for any pharma project manager. The project will also include the input of consultancy, contractor and regulatory representatives.

However, national and regional authorities are desperate to attract pharmaceutical companies, and they are preoccupied with creating and rolling out financial and other incentives aimed at drawing these companies in. The reasons are simple: the pharmaceutical business has an economic multiplier effect; jobs tend to receive higher remuneration than other parts of the manufacturing sector and, from an environmental point of view, its manufacturing tends to have a lighter impact.

Site enticements

A report from the Pharmaceutical Research and Manufacturers of America, produced by the Milken Institute, an economic think tank based in Santa Monica, California, US, found that each job created by biopharma creates an additional 5.7 jobs in the overall economy. This may explain why, in the US at least, states are competing more heavily than ever for site selection.

According to statistics gathered by business services firm Deloitte, at least 40 states in the US now have R&D tax credits and sales, and use tax exemptions, investment tax credits or economic development grants for life sciences. Over 25 states have initiated publicly backed venture funds that inject cash into bioscience-related activities and 16 are using funds from multistate tobacco settlements to finance bioscience R&D.

One of the tax breaks to appear in recent years, according to Deloitte, is net operating loss (NOL), which allows companies to sell into financial markets the operating losses they incur

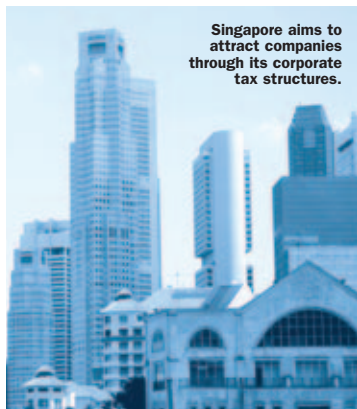
while starting up, before they make enough profit to offset the loss themselves. The scheme, devised by the State of New Jersey, enables the originating company of the NOL to convert some of that lost tax credit into additional funds; the company buying the credit is able to use it to offset current profits, but at a cost less than if it had incurred the loss itself.

Labour considerations

Checking the employment figures is a good way to start the assessment of sites, because an essential factor – the locations of major research centres and universities – determines much of what follows in the process. The logic is that manufacturing comes out of the commercialisation of research, and the location of a research facility will eventually lead to the location of job-generating manufacturing operations. ‘When considering a new site, it’s just not practical to import talent from overseas, so we rate the availability of a skilled local labour force as one of our key criteria,’ explains Eduardo von Achenbach, global head of pharmaceutical operations at Novartis’ TechOps unit in Switzerland.

Novartis has launched a new site in Singapore, to begin operation this year, a chemical production and development plant in China, and a new site near Istanbul, Turkey. However, these all required a great deal of forward planning. ‘You have to be aware of the labour laws,’ says von Achenbach. ‘If you decide to leave years later, there may be some restrictions or penalties, so you need to be aware of these details from the beginning.’

The quality of labour pools has also worked well for California and Massachusetts, strong hubs for academic research where many noted discoveries in biotechnology have been made. North Carolina’s investments in the Research Triangle Park complex have also paid off with new sitings for biotech and pharmaceutical research. The economic development boards of a number of other states have now reassessed educational and research foundations, and are promoting them as candidate locations for siting pharmaceutical research and



manufacturing. In New York State, the Buffalo Niagara economic development authority touts the presence of the State University of New York as a draw. 'Our region, in partnership with New York State, made the decision to seriously focus on the life sciences sector more than 15 years ago, and has increasingly made significant investments in research, buildings, research scientists, and creation of industry clusters during the last ten years,' says David Tyler, SUNY Buffalo programme manager. 'The state has designated SUNY Buffalo as a Centre of Excellence in Bioinformatics; we're also a strong centre for clinical trials.'

Tyler cites another advantage of the Buffalo area: its proximity to Canada. Having easy access from both sides of the border allows companies to engage in two markets from the same location. 62% of the Canadian and 55% of the US population reside within 500 miles of the Buffalo Niagara region. At least one pharmaceutical company, Lamm Pharmaceutical, decided to split the difference by having its headquarters in Toronto and its R&D operations in Buffalo. The topic is controversial given concerns about drug importation from Canada but, from pharma's perspective, ready access to the markets of two countries is always a plus. Buffalo boasts more than 130 life sciences companies, including Invitrogen and Greatbatch, that employ a total of around 7,500 people.

Follow the rules

As for the impact of laws and regulations on site expansion or construction, there are sharply differing views. According to Carlo de Notaristefani, president of Technical Operations, the supply organisation for Bristol-Myers Squibb, regulation affecting site location has grown tight and complex in recent years and, frustratingly, increasingly disconnected. 'As a result of each country putting in place its own GMP regulations, we have a situation where there is less standardisation and global acceptance,' says de Notaristefani. 'The landscape is now highly fragmented.' Regulatory health authorities often inspect a particular company or manufacturing site on behalf of their country. This can result in multiple inspections of a particular site by many regulatory health authorities. Importation testing and supplementary local testing can be a requirement within specific countries in order to approve a new product in a given area. This can result in unnecessary costs and constrain supply, without adding to product quality.'

He agrees that the availability of talent and manufacturing and operational costs are the two biggest factors affecting site selection. However, these are often in conflict. For example, in the case of biologics, talent is focused on the east and west coasts of the US – the higher cost regions in the country. Technical Operations recently embarked on a site selection assessment for building its new biologics facility, and

finally settled on Devens, Massachusetts, because, according to de Notaristefani, 'it aligned most closely with our criteria, which included our ability to attract and retain a qualified workforce, the suitability of a building site, the business and regulatory environment and overall economics'.

Selection drivers

Matt Szuhaj, director for strategy and operations at Deloitte, confirms that life sciences companies typically focus on mitigating financial, regulatory and operational risks when developing a location strategy and deploying manufacturing facilities. But he cites IP protection, from both a regulatory and enforcement perspective, as another important consideration.

Also on the shopping list is a stable political, regulatory and economic environment, reduced exposure to the risk of natural disasters or social upheaval, an ability to regionalise the product mix if necessary, and the availability of a flexible manufacturing capacity with suitable lead times and low supply chain costs. Tax is one of the priorities in the selection process. 'Locations with suitable operating conditions, meaning the availability of the right labour, adequate infrastructure, available sites, and attractive corporate tax structures, are frequently considered for manufacturing operations,' says Szuhaj. 'Traditionally, this included Republic of Ireland, Puerto Rico, Switzerland and Singapore. Other ascending eastern European and Asian countries have established tax incentives, but mainly for R&D. However, tax benefits are hugely impacted by a company's corporate and tax structure, so the financial impact can vary widely by company.'

The number of products achieving approval has declined, with only a handful making it to market.

Long-term impact

Stephen Taylor, chair of bioProcess UK, one of the UK government's knowledge transfer networks, and a director at Avecia, believes the initial decision to make a huge investment in site expansion or new site construction is the hardest part of the process. 'You have to make choices about expansion of assets or new assets on an incredibly long time-line,' he explains. 'The average is around two years by the time you've done the building, qualification, validation and handled the regulatory processes you have to go through if you're making drugs. To build something on a new location can easily take four years.'

There are also huge risks involved in pushing a product through development and getting it to market. 'You can't readily change where you're manufacturing,' he adds. 'The facilities used for making products later in development will be the same as the ones you use to make licensed commercial products. That's the way biologics are regulated. Since the manufacturing locations are typically part of the overall package that gets approved, you have to plan far in advance.'

The situation used to be worse, according to Taylor, who welcomes the fact that regulators now recognise such peculiarities as multi-product facilities, which was unknown at the dawn of biologics. They also now recognise the role of contract manufacturers. 'The holder of the product licence can be different from the site of manufacturing, but in the early days that wasn't the case,' he says. 'So, to be fair, there have been some positive changes.'

Recently, the number of products achieving approval has declined, with only a handful making it to market last year. 'The regulators are becoming stricter in how they look at products,' says Taylor. 'You're making large investment decisions about facilities for manufacturing when products are still in development, in an environment where fewer products than ever are getting to market. Against this background, the decision to build or expand is actually the most difficult of all.'

Green debate

Taylor doesn't see environmental issues impacting heavily on site selection or construction. 'With biologics you're not dealing with a toxic waste product, so the discharge of nasty materials isn't an issue,' he says. 'But you have to deal with microorganisms, and in some parts of the world that's harder.'

In Japan it's still difficult manufacturing with certain GMOs because there are some hurdles that are tougher to clear.'

De Notaristefani also refutes the idea that environmental issues have been a limiting factor for the pharmaceutical industry. 'Historically, the industry has been environmentally friendly and new regulations have not prevented us from expanding our facilities,' he says. 'One factor that may limit expansion is the availability of natural resources; for example, water in the case of biologics production.'

The design of new facilities includes environmental protection factors to ensure minimal impact over the life of the facility. This then guarantees an easy decommissioning.

Looking ahead

With the cost of developing a new drug approaching \$1 billion, writing off a once-promising treatment can be a tremendously costly affair. It's just as well that pharmaceutical companies are among the most sophisticated businesses in terms of being able to maximise shareholder value, manage regulation and evaluate economic incentives. It's important that they apply this hard-gained knowledge and experience to site selection in order to get the most from their new manufacturing or R&D base, and avoid pitfalls and problems further down the line. **WPF**



MECALAB Isolator Glove Box Systems

MECALAB, part of the MBRAUN Group has long-standing experience in developing, designing and producing barrier isolator systems and containment solutions for the pharmaceutical industry.

We offer optimally designed solutions for research, development and production. Our product range starts from standard isolator systems for product and/or user protection, including a full range of accessories, and extends to fully customised production systems.

We have a wide experience of connecting isolator systems to filter dryers, freeze dryers, reactors and other production units, as well as in the integration of mills,

filling machines, mixers and all kinds of automated or robotic systems. We can also supply EX-certified systems for EX zone 1.

Our depth of experience in the market allows us to support qualification and validation needs, including the necessary documentation and on-site support.

MECALAB-M.BRAUN AG

Bündengasse 22, CH-2540 Grenchen, Switzerland

Tel: +41 (0) 32 654 22 66

Fax: +41 (0) 32 654 22 77

Email: info@mecalab.com